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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,683	05/04/2001	Rebanta Bandyopadhyay	3479	8928

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EXAMINER	
JONES, DWAYNE C	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,683	BANDYOPADHYAY ET AL.	
	Examiner	Art Unit	
	Dwayne C Jones	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *the amendment of 23 JAN 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-11,13-15 and 17-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-11,13-15 and 17-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/21/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1, 4-11, 13-15, and 17-39 are pending.

2. Claims 1, 4-11, 13-15, and 17-39 are rejected.

Information Disclosure Statement

3. The information disclosure statement filed May 21, 2002 has been reviewed and considered, see enclosed copy of PTO FORM 1449.

Response to Arguments

4. Applicant's arguments with respect to claims 1, 4-11, 13-15, and 17-39 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 4-11, and 13-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the ocular COX-2 mediated disorders of blepharitis, post-operative inflammation and pain form corneal transplant surgery, endophthalmitis, episcleritis, keratitis, keratoconjunctivitis, keratoconjunctiviitis sicca, post-operative inflammation and pain from lens implantation surgery, Mooren's

ulcer and post-operative inflammation and pain from retinal detachment surgery, does not reasonably provide enablement for other types of ocular COX-2 mediated disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The instant invention is directed to using COX-2 inhibitors treat ocular COX-2 mediated disorders of blepharitis, post-operative inflammation and pain form corneal transplant surgery, endophthalmitis, episcleritis, keratitis, keratoconjunctivitis, keratoconjunctiviitis sicca, post-operative inflammation and pain from lens implantation surgery, Mooren's ulcer and post-operative inflammation and pain from retinal detachment surgery.

(2) The state of the prior art

The compounds of the inventions are COX-2 inhibitors. However, the prior art does not teach that these all COX-2 inhibitors can treat all ocular COX-2 mediated disorders, see Miyake et al. of WO 99/59634.

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements functioning the same in different circumstances, yielding predictable results, but chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. Supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24 (CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5 (BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotropic hormones was unpredictable art; In re Wright, 999 F.2d 1557, 1562, 29 USPQ d, 1570, 1513-14

(Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of using COX-2 inhibitors prior to filing of the instant invention was an unpredictable art.

(5) The breadth of the claims

The instant claims are very broad. For instance, claim 1 is directed to the plethora of ailments or disorders that are mediated by COX-2. The breadth of claims was a factor in Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d (Fed. Cir.),cert. Denied, 502 U.S. 856 (1991). In the Amgen case, the patent claims were directed to DNA sequences that encoded amino acid sequences. Because a very small change in the amino acid sequence of a protein can result in a very large change in the structure-function activity of a protein and because the laws of protein folding are in such a primitive state, predicting protein structure (and hence, activity) while knowing only the sequence of the protein is akin to predicting the weather for a date in the future.

(6) The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving

unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fischer, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. In the instant case, given the unpredictability of the physiological or pharmaceutical activity of a COX-2 inhibitor to be effective in treating ocular COX-2 mediated disorders is insufficient for enablement. The specification provides no guidance, in the way of enablement for all COX-2 mediated disorders other than using COX-2 inhibitors treat ocular COX-2 mediated disorders of blepharitis, post-operative inflammation and pain form corneal transplant surgery, endophthalmitis, episcleritis, keratitis, keratoconjunctivitis, keratoconjunctiviitis sicca, post-operative inflammation and pain from lens implantation surgery, Mooren's ulcer and post-operative inflammation and pain from retinal detachment surgery. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Accordingly, this is because it is not obvious from the disclosure of one species, what other species will work. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must

appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in detail. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds that fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

(7) The presence or absence of working examples

As stated above, the specification discloses COX-2 inhibitors that have the ability to treat all ocular COX-2 mediated disorders. However, the instant specification only has enablement for using COX-2 inhibitors treat ocular COX-2 mediated disorders of blepharitis, post-operative inflammation and pain form corneal transplant surgery, endophthalmitis, episcleritis, keratitis, keratoconjunctivitis, keratoconjunctiviitis sicca, post-operative inflammation and pain from lens implantation surgery, Mooren's ulcer and post-operative inflammation and pain from retinal detachment surgery

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in determining whether "undue experimentation" is

required to make and use the instant invention. "'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of the all ocular COX-2 mediated disorders that would be enabled in this specification.

7. Claims 17-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of the ocular COX-2 mediated disorders of blepharitis, post-operative inflammation and pain form corneal transplant surgery, endophthalmitis, episcleritis, keratitis, keratoconjunctivitis, keratoconjunctiviitis sicca, post-operative inflammation and pain from lens implantation surgery, Mooren's ulcer and post-operative inflammation and pain from retinal detachment surgery, does not reasonably provide enablement for prevention of the ocular COX-2 mediated disorders of blepharitis, post-operative inflammation and pain form corneal transplant surgery, endophthalmitis, episcleritis, keratitis, keratoconjunctivitis, keratoconjunctiviitis sicca, post-operative inflammation and pain from lens implantation surgery, Mooren's ulcer and post-operative inflammation and pain from retinal detachment surgery. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Nature of the Invention, State of the Prior Art, Relative Skill of those in the Art, and The Predictability of the Art

The nature of the invention is directed to using COX-2 inhibitors to **prevent** the ocular COX-2 mediated disorders of blepharitis, post-operative inflammation and pain form corneal transplant surgery, endophthalmitis, episcleritis, keratitis, keratoconjunctivitis, keratoconjunctiviitis sicca, post-operative inflammation and pain from lens implantation surgery, Mooren's ulcer and post-operative inflammation and pain from retinal detachment surgery.

The claimed invention relates to methods of treating a patient with COX-2 inhibitors to **prevent** the ocular COX-2 mediated disorders, listed above.

The relative skill of those in the art is generally that of a PhD candidate or PHD.

The Breadth of the Claims

The claims are very broad and inclusive of any and all methods of administering COX-2 inhibitors for the **prevention** of the ocular COX-2 mediated disorders, stated above.

The Amount of Direction of Guidance provided and The Presence or Absence of Working Examples

The specification provides no direction for ascertaining which COX-2 inhibitors can be used for the **prevention** of the ocular COX-2 mediated disorders, listed above.

Only a limited selection of specified COX-2 inhibitors are shown to treat rather than to **prevent** the ocular COX-2 mediated disorders, cited above.

The Quantity of Experimentation Necessary

Applicant fails to provide guidance and information sufficient to allow one skilled in the art to ascertain how COX-2 inhibitors **prevent** the ocular COX-2 mediated disorders, cited above, without resorting to undue experimentation. The skilled artisan would expect the interactions of a particular COX-2 inhibitor with its receptor to have a range of specificity, which may or may not be effective in the treatment -- let alone the prevention -- of ocular COX-2 mediated disorders. In addition, this interaction between a particular COX-2 inhibitor with its receptor would be highly unpredictable absent a clear understanding of the structural and biochemical basis for each and the instant specification sets forth no such understanding nor any criteria for extrapolating beyond those actually demonstrated. In the absence of a reasonable a priori expectation of success for using a COX-2 inhibitor to **prevent** the ocular COX-2 mediated disorders, cited above, one skilled in the art would have to extensively test how these ailments or disorders that are mediated by COX-2 are in fact prevented.

The term "preventing" is synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Since the absolute success of preventing COX-2 mediated disorders, cited above, such as ocular pain, is not possible, the specification is viewed as lacking an adequate written description that is enabling for **preventing** the ocular COX-2 mediated disorders, cited above, with

COX-2 inhibitors. The examiner recommends replacing "preventing" with "reducing" or something equivalent for which applicants have support.

Obviousness-type Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
9. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).
10. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. The provisional rejection of claims 1, 4-11, 13-15, and 17-39 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 40 of copending Application No. 09/904,098 is maintained and repeated. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are directed to the treatment of COX-2 mediated disorders of the eye with the administration of a selective COX-2 inhibitor.

12. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (571) 272-

0578. The examiner can normally be reached on Mondays, Tuesdays, Thursday, and Fridays from 8:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, may be reached at (571) 272-0951. The official fax No. for correspondence is (703) 872-9306.

Also, please note that U.S. patents and U.S. patent application publications are no longer supplied with Office actions. Accordingly, the cited U.S. patents and patent application publications are available for download via the Office's PAIR, see http://pair-direct.uspto.gov. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources.

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DWAYNE JONES
PRIMARY EXAMINER
Tech. Ctr. 1614
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